

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A method for screening a candidate compound for its ability to interact with at least one transmembrane protein comprising:

transfected a cell with at least one nucleotide sequence encoding a protein comprising a transmembrane protein containing at least one nuclear localisation sequence (NLS) and a detectable moiety and permitting expression of the encoded protein in the cell;

contacting the cell with a candidate compound; and

determining the distribution of the expressed protein in the cell by detecting the distribution of the detectable moiety in the cell;

wherein detection of an altered distribution of the detectable moiety in the cell relative to the distribution of the detectable moiety in a control cell not contacted with the candidate compound indicates that the compound interacts with the transmembrane protein; and

wherein the wild type transmembrane protein lacks an NLS and the nucleotide sequence encoding the transmembrane protein is modified to encode an NLS.

2. (Previously Amended) The method of claim 1 wherein the detectable moiety is a detectable peptide comprising an antigenic portion of the amino acid sequence of the transmembrane protein and/or wherein the nucleotide sequence encodes a fusion protein comprising a transmembrane protein containing at least one NLS and a detectable moiety.

3. (Previously Canceled)

4.-5. (Canceled Herein)

6. (Currently Amended) The method of claim 1 5 wherein the nucleotide sequence is modified to encode an NLS selected from Table 1 or wherein the nucleotide sequence is modified to encode an amino acid sequence selected from the group consisting of KKFKR (SEQ ID NO: 158), PKKKRKV (SEQ ID NO: 154) and AFSAKKFKR (SEQ ID NO: 159).

7. (Previously Canceled)

8. (Currently Amended) The method of claim 1 wherein the cell is a prokaryotic cell or a eukaryotic cell selected from the group consisting of a mammalian cell, optionally selected from the group consisting of HEK, COS and CHO cells, a yeast cell, an insect cell, a nematode cell, a plant cell and a fungal cell.

9.-10. (Previously Canceled)

11. (Currently Amended) The method of claim 2 wherein the detectable moiety is an antigenic peptide and the distribution of the antigenic peptide in the cell is determined by allowing it to bind to an antibody-based detection system comprising an antibody specific for the antigenic peptide, optionally selected from the group consisting of an antibody-based detection system comprising a first antibody specific for the antigenic peptide and a second antibody carrying a detectable label and specific for the first antibody or and an antibody-based detection system comprising a first antibody specific for the antigenic peptide and carrying a detectable label, optionally wherein the detectable label is selected from the group consisting of an optically detectable label, optionally a luminescent and or a fluorescent label.

12-15. (Previously Canceled)

16. (Currently Amended) The method of claim 2 3 wherein the detectable moiety is a polypeptide selected from the group consisting of green fluorescent protein, red fluorescent protein and modified variants thereof.

17. (Previously Amended) The method of claim 1 wherein the transmembrane protein is selected from the group consisting of a G protein coupled receptor (GPCR), a transporter, a cytokine receptor, a tyrosine kinase receptor and a low density lipoprotein (LDL) receptor.

18. (Original) The method of claim 17 wherein the transmembrane protein is a GPCR.

19. (Currently Amended) The method of claim 18 wherein the GPCR is selected from the group consisting of a dopamine D1 receptor, a dopamine D2 receptor, a dopamine D3 receptor, a dopamine D5 receptor, a histamine 1 receptor, a cysteinyl leukotriene receptor 1, a cysteinyl leukotriene receptor 2, an opioid receptor, a muscarinic receptor, a serotonin receptor, a beta2-adrenergic receptor and a metabotropic glutamate 4 receptor.

20. (Currently Amended) The method of claim 17 wherein the transmembrane protein is a transporter selected from the group consisting of a dopamine transporter and a serotonin transporter, a cytokine receptor selected from the group consisting of an erythropoietin receptor and an insulin receptor, a tyrosine kinase receptor selected from the group consisting of an epidermal growth factor receptor and an insulin receptor, and or a low density lipoprotein receptor.

21-26. (Previously Canceled)

27. (Previously Amended) The method of claim 1 wherein the cell is transfected with a plurality of nucleotide sequences, each of said sequences encoding a protein comprising a different transmembrane protein containing at least one NLS and wherein each of said nucleotide sequences encodes a protein comprising a different detectable moiety or wherein at least one detectable moiety is common to at least two encoded proteins.

28-29. (Previously Canceled)

30. (Original) The method of claim 1 wherein the cell is contacted with a compound known to interact with the at least one transmembrane protein prior to contacting the cell with the candidate compound and

wherein detection of an altered distribution of the detectable moiety in the cell relative to the distribution of the detectable moiety in a control cell contacted with the compound known to interact with the transmembrane protein but not contacted with the candidate compound indicates that the candidate compound interacts with the transmembrane protein.

31. (Previously Amended) The method of claim 1 wherein detection of an altered distribution of the detectable moiety in the cell comprises detection of a reduced level or an increased level of the detectable moiety associated with the cell membrane.

32-33. (Previously Canceled)

34. (Previously Amended) The method of claim 1 wherein detection of an altered distribution of the detectable moiety in the cell comprises detection of a reduced level or an increased level of the detectable moiety in the nucleus of the cell.

35-36. (Previously Canceled)

37. (Withdrawn, Currently Amended) A method for screening a candidate compound for its ability to interact with at least one transmembrane protein comprising:

transfected a cell with at least one nucleotide sequence encoding an NLS-containing transmembrane protein and permitting expression of the encoded protein in the cell;

contacting the cell with a candidate compound; and

determining the level of NLS-containing transmembrane protein remaining at the cell membrane by isolating the cell membrane fraction of the cell, contacting the fraction with a labelled ligand of the transmembrane protein and determining the level of binding of the ligand to the fraction;

wherein detection of an altered level of the transmembrane protein at the cell membrane relative to the level at the cell membrane in a control cell not contacted with the candidate compound indicates that the compound interacts with the transmembrane protein, and

wherein the wild type transmembrane protein lacks an NLS and the nucleotide sequence encoding the transmembrane protein is modified to encode an NLS.

38. (Withdrawn) The method of claim 37 wherein the labelled ligand is a radio-labelled ligand.

39.-40. (Canceled Herein)

41. (Withdrawn, Currently Amended) The method of claim 37 40 wherein the nucleotide sequence is modified to encode an NLS selected from Table 1 or wherein the nucleotide sequence is modified to encode an amino acid sequence selected from the group consisting of KKFKR, PKKKRKV and AFSAKKFKR.

42. (Previously Canceled)

43. (Withdrawn, Currently Amended) The method of claim 37 wherein the cell is a prokaryotic cell or a eukaryotic cell selected from the group consisting of a mammalian cell, ~~optionally selected from the group consisting of HEK, COS and CHO cells, a yeast cell, an insect cell, a nematode cell, a plant cell and a fungal cell.~~

44-45. (Previously Canceled)

46. (Withdrawn, Previously Amended) The method of claim 37 wherein the transmembrane protein is selected from the group consisting of a G protein coupled receptor (GPCR), a transporter, a cytokine receptor, a tyrosine kinase receptor and a low density lipoprotein (LDL) receptor.

47. (Withdrawn) The method of claim 46 wherein the transmembrane protein is a GPCR.

48. (Withdrawn, Currently Amended) The method of claim 47 wherein the GPCR is selected from the group consisting of a dopamine D1 receptor, a dopamine D2 receptor, a dopamine D3 receptor, a dopamine D5 receptor, a histamine 1 receptor, a cysteinyl leukotriene receptor 1, a cysteinyl leukotriene receptor 2, an opioid receptor, a muscarinic receptor, a serotonin receptor, a beta2-adrenergic receptor, and a metabotropic glutamate 4 receptor.

49. (Withdrawn) The method of claim 46 wherein the transmembrane protein is a transporter selected from the group consisting of a dopamine transporter and a serotonin transporter, a cytokine receptor selected from the group consisting of an erythropoietin receptor and an insulin receptor, a tyrosine kinase receptor selected from the group consisting of an epidermal growth factor receptor and an insulin receptor, and or a low density lipoprotein receptor.

50-55. (Previously Canceled)

56. (Withdrawn, Previously Amended) The method of claim 37 wherein the cell is transfected with a plurality of nucleotide sequences; each of said sequences encoding a protein comprising a different transmembrane protein containing at least one NLS and wherein each of said nucleotide sequences encodes a protein comprising a different detectable moiety or wherein at least one detectable moiety is common to at least two encoded proteins.

57-58. (Previously Canceled)

59. (Withdrawn, Previously Amended) The method of claim 37 wherein detection of an altered distribution of the detectable moiety comprises detection of a reduced level or an increased level of the detectable moiety associated with the cell membrane.

60. (Previously Canceled)

61.-62. (Canceled Herein)

63. (Previously Canceled)

64.-66. (Cancelled Herein)

67. (Previously Canceled)

68. (Cancelled Herein)

69-72. (Previously Canceled)

73.-77. (Canceled Herein)

78-83. (Previously Canceled)

84. (Cancelled Herein)

85-86. (Previously Canceled)

87. (Cancelled Herein)

88-89. (Previously Canceled)

90.-93. (Canceled Herein)

94-95. (Previously Canceled)

96.-97. (Canceled Herein)

98. (Previously Canceled)

99.-101. (Canceled Herein)

102. (Previously Canceled)

103. (Canceled Herein)

104-105. (Previously Canceled)

106. (Canceled Herein)

107-111. (Previously Canceled)

112.-115. (Canceled Herein)

116-121. (Previously Canceled)

122. (Canceled Herein)